

Children's Safe Products Act
Rationale for Chemicals listed under Reporting Requirements
Submitted April 18, 2011

Introduction

The criteria and process for selecting chemicals for the list of Chemicals of High Concern to Children (CHCC) are described in the CSPA law (Chapter 70.240 RCW) and the Phase 1 and Phase 2 prioritization procedures on the Department of Ecology's web site (<http://www.ecy.wa.gov/programs/swfa/rules/ruleChildPilotPhase.html>).

Briefly, the CSPA law defines criteria for including chemicals on the CSPA reporting list. As written, these criteria are very broad, with potentially thousands of chemicals meeting the definition of "high priority chemicals that are of high concern for children" (i.e., a combination of the criteria in 70.240.010(6) RCW and 70.240.030(1) RCW). Phase 2 was used to narrow the list to a number consistent with the Governor's direction. The Department of Health (DOH) consulted with Ecology during the development of the list. Ecology determined what sources of information were considered authoritative. The agencies consulted with University of Washington Pediatric Environmental Health Specialty Unit (PEHSU) to determine what types of information about toxicity and exposure would be evaluated and what specific criteria would be used to select the chemicals for the reporting list. Ecology in consultation with University of Washington Pediatric Environmental Health Specialty Unit (PEHSU) developed scoring sheets to help prioritize chemicals for inclusion on the list.

As part of the Phase 3 process, DOH was asked by Ecology to review the draft CSPA reporting list to ensure that all chemicals proposed for the final list met the criteria of the CSPA law as well as Ecology's Phase 2 selection criteria. With the few exceptions noted in the Phase 3 report, DOH confirmed that most of the chemicals on the draft list did meet the criteria of both the CSPA law and Phase 2. Any that didn't were eliminated. It should be noted that the draft CSPA reporting list contains chemicals with a wide variety of toxicity and exposure profiles. Some chemicals are very potent while others appear to require large doses for any effect. Some chemicals were widely found in children's products while others had limited evidence of exposure potential. We also found that many listed chemicals had other endpoints of concern (e.g. neurotoxicity, respiratory irritation, dermal sensitization) that occurred at lower concentrations than the endpoints prioritized in Phase 2 (i.e., cancer and adverse effects on reproduction, fetal/child development, and the endocrine system).

In this report, DOH provides brief summaries of the toxicity and exposure information for each listed chemical. The summaries do not represent comprehensive reviews of the literature, but are meant to supply sufficient information to show that the chemicals meet the criteria of the law and Ecology's selection process. DOH was not asked to conduct health risk assessments or eliminate chemicals with evidence of toxicity only at high doses. The law did not require, nor did Ecology's ranking criteria include, consideration of dose-response information or evaluation of the amount of exposure likely to

come from children's products when prioritizing chemicals for the list. As such, DOH and Ecology do not assume the chemicals on the CSPA list to be hazards when present in children's products. Some chemicals may not be particularly accessible or may be present in concentrations unlikely to cause harm.

Currently, agencies entrusted with protecting children's health lack adequate information about the use of chemicals in products, making it difficult to evaluate the potential for exposure and, consequently, the potential for harm. The information that can be collected under the CSPA law can help agencies and the public gain a better understanding of what chemicals are in the products they use and help us evaluate whether or not there is a hazard and, if so, what could be done about it.

With regard to carcinogenic chemicals, Ecology in consultation with University of Washington Pediatric Environmental Health Specialty Unit (PEHSU) defined authoritative sources in Phase 2. When we state that a "chemical is classified as a carcinogen by authoritative sources" in the following summaries, we are referring to five entities identified in phase 2: International Agency for Research on Cancer (IARC), the U.S. National Toxicology Program, the U.S. Environmental Protection Agency, the European Commission, Joint Research Center, Institute for Health and Consumer Protection, and the State of California List of Proposition 65 Chemicals. The specific cancer ratings required for inclusion on the CHCC list are described in the Phase 2 report.

With regard to endocrine disruptors, the CSPA allows a chemical to be included if it is known to "disrupt the endocrine system" (70.240.010(6)(c) RCW). For phase 2 Ecology refined this criterion to prioritize Category 1 chemicals on the European Union's list of endocrine disruptors. Research into the endocrine disrupting effects of chemicals is evolving rapidly, and questions have been raised about the use of the European Union list of endocrine disruptors for selecting CHCCs. Therefore DOH collaborated with the University of Washington Pediatric Environmental Health Specialty Unit (PEHSU) to review chemicals included on the CHCC list only for endocrine disruption. A variety of experimental protocols (assays) have been used to identify chemicals that can disrupt the endocrine system. These range from *in vitro* receptor binding assays to multi-generation studies of development and reproduction in mammals. All the chemicals that were included in the CHCC list only because of endocrine disruption have been shown to disrupt the endocrine system based on the results of one or more relevant assay.

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CAS 50-00-0

Substance name Formaldehyde

Toxicity

Formaldehyde is classified as a carcinogen by a number of authoritative sources.^{1,2,3,4} Inhalation of formaldehyde is associated with cancer in the respiratory tract in humans and laboratory animals. Oral exposures in animals are also carcinogenic. Formaldehyde is a skin, eye and respiratory tract irritant and sensitizer.

Exposure

Formaldehyde is used in the production of resins which are commonly used as adhesives and binders in wood products, pulp and paper, and in the production of plastics and coatings. It is also used in the finishing treatment of fabrics used in clothing and other products.⁵ Aqueous formaldehyde (formalin) is used as a preservative and antimicrobial agent in some soaps, shampoos, hair preparations, deodorants, lotions, cosmetics and nail products.⁶ Some of these may be marketed to children. Formaldehyde has been detected in a wide range of children's products including feeding pillows, nursing pillows, glitter glues, infant mittens, infant jackets, disposable diapers, bed linens, children's tents, and glue sticks.⁷

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Substance name Aniline

Toxicity

Aniline is classified as a carcinogen by a number of authoritative sources.^{1,2,3} Tumors of the spleen are observed in test animals. Bladder cancers have been reported in occupationally exposed groups but co-exposures with other chemicals limits conclusions. Animal testing also shows that aniline damages red blood cells and causes toxic effects in the blood system (i.e., spleen, bone marrow, kidney, and liver).² Overexposure in humans causes methemoglobinemia and cyanosis.^{2,4}

Exposure

Aniline is used primarily as a chemical intermediate in production of MDA (methylene di-aniline), a starting product for polyurethane plastics. In the rubber industry, aniline is used in the manufacture of antioxidants and rubber accelerators. It is also used in the manufacture of dyes, agricultural chemicals, optical whitening agents, resins, marking inks, perfumes, and certain pharmaceuticals. Aniline has been an ingredient in household products including shoe polish and inks.^{2,4,5}

Aniline has been detected in a variety of children's products including balloons, marker pens, infant bed linens, and the outer material of an infant jacket.⁶ The CDC has not assessed whether aniline is present in peoples' bodies in the U.S. but biomonitoring in the general population of Bavaria showed detectable levels of aniline in urine of 94% of participants.⁷ Aniline detected may be from degradation of polyurethane plastics.

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Substance name N-Nitrosodimethylamine (NDMA)

Toxicity

N-Nitrosodimethylamine is classified as a carcinogen by a number of authoritative sources based on animal evidence of liver, kidney and lung tumors after oral, inhalation or injection exposures. Exposure to rodents during pregnancy resulted in tumors in offspring.^{1,2,3,4}

Exposure

Nitrosamines can be formed as process contaminants when carbamate chemicals are used during rubber production.⁵ According to the National Toxicology Program, it is also used as a plasticizer for rubber and acrylonitrile polymers and as a solvent in the fiber and plastics industry.² NDMA has been detected in children's products including silicone and natural rubber baby bottle nipples and pacifiers,^{5,6} balloons,^{7,8,9} and personal care products such as baby shampoo and bath foam.⁹

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CAS 71-36-3

Substance name n-Butanol

Toxicity

Workplace exposures to n-butanol have been associated with eye, nose and throat irritation and neurological effects such as dizziness, vertigo, and hearing impairment.^{1,2} It is classified by Reprotext as a “A-” reproductive hazard.³ In animals, fetotoxicity and teratogenicity was observed at high doses by both the inhalation and oral routes of exposure.^{4,5,6,7}

Exposure

N-butanol is a widely used industrial solvent used for paints, lacquers, varnishes, resins and dyes.² Product testing by the Danish government detected n-butanol in several categories of children’s products including slimy toys, children’s tents, coatings on wooden toys, and a scented rubber toy.⁸ N-butanol is listed as an ingredient in paints, sharpie markers, dry erase markers, and nail products in the National Library of Medicine Household Products Database.⁹ N-butanol occurs naturally as a product of carbohydrate fermentation and is present in food.¹⁰

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Toxicity

Benzene is considered a known human carcinogen by authoritative sources.^{1,2,3} All routes of exposure are considered carcinogenic based on convincing occupational evidence and supporting evidence from animal studies.⁴ Benzene is toxic to blood cells. Evidence in animals suggests that exposure to benzene *in utero* can alter fetal maturation of lymphocytes, erythrocytes, and granulocytes and that the damage to the hematopoietic system during development can last into adulthood.⁵

Exposure

Biomonitoring by the CDC shows that benzene exposure is widespread in the U.S. population.⁶ Vehicle exhaust and cigarette smoke are common sources of exposure. Benzene is also used in the manufacture of plastics, synthetic rubber, dyestuffs, resins, raw materials for detergents, and plant protection agents.³ Testing by the Danish EPA found quantifiable benzene in one out of four balloons tested and in two scented children's toys.⁷ Benzene was found infrequently in a large study of common household products in the USA.⁸

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CAS 75-01-4

Substance name Vinyl chloride

Toxicity

Vinyl chloride is classified as a human carcinogen by authoritative sources.^{1,2,3} Evidence indicates that it causes liver and other cancers in occupationally exposed people and in test animals.¹ Vinyl chloride is considered mutagenic and genotoxic.¹ Young animals are particularly prone to the formation and persistence of vinyl chloride-induced adducts and are more likely than adults to develop tumors.⁴

Exposure

Vinyl chloride is used primarily to make polyvinyl chloride (PVC). Children's products such as bath toys, squeeze toys, and dolls are often made from PVC. PVC can be softened with plasticisers into the plastic commonly known as vinyl. Vinyl is used in numerous children's products including inflatable pools, inflatable play structures, play mats, clothing, mattress covers, and bibs. Chewing or sucking on these products has the potential to release any unpolymerized vinyl chloride from the object.⁴ We did not locate product testing data for vinyl chloride monomer from children's products.

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CAS 75-07-0

Substance name Acetaldehyde

Toxicity

Acetaldehyde is classified as a carcinogen by authoritative sources.^{1,2,3} Prolonged inhalation exposure causes nasal cancers in test animals. Human evidence from workplace exposures is supportive but not conclusive.² Acetaldehyde is a major metabolite of ethanol in mammals and may be involved in fetal alcohol syndrome. For this reason, Reprotext classifies acetaldehyde as an A- unconfirmed human reproductive hazard.⁴

Exposure

Acetaldehyde is used primarily as a feedstock in the production of other chemicals. Other uses are or have been in leather tanning, in glues, in the paper industry, in the manufacture of cosmetics and plastics, and as a food flavoring agent.^{1,4} Acetaldehyde was detected in 6 out of 6 children's tent samples in testing by the Danish EPA.⁵ Acetaldehyde is listed as an ingredient in school glue and other arts and craft glues in the NLM Household Products Database.⁶

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Substance name Methylene chloride (also called dichloromethane)

Toxicity

Methylene chloride is classified as a carcinogen by authoritative sources.^{1,2,3} Inhalation exposures in laboratory animals result in lung and liver cancers and mammary gland tumors.² Methylene chloride is metabolized to carbon monoxide in mammals.³ Because carbon monoxide increases the levels of carboxyhemoglobin in the blood and is a known reproductive hazard, Reprotext classifies methylene chloride as a Class A+ reproductive hazard.⁴

Exposure

Methylene chloride is used as an industrial solvent in paint removers and degreasers, as a carrier solvent in the textile industry, and as a blowing agent in foam production. It is used in inks and adhesives and in plastics manufacture, as an extraction solvent for spices and hops, and is used to extract caffeine from coffee.^{1,2,5} Methylene chloride is also used in spray shoe polish and water repellent and in wood stains, varnishes and finishes.² It was detected in 1 of 14 slimy toys tested by the Danish EPA.⁷

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CAS 75-15-0

Substance name Carbon disulfide

Toxicity

Carbon disulfide is neurotoxic and is identified as a reproductive and developmental toxicant by authoritative sources.¹⁻⁵ Evidence comes from laboratory animal testing as well as supportive data from epidemiological studies of workplace exposures in men and women.

Exposure

Carbon disulfide is a thermal decomposition product of zinc dibutyldithiocarbamate, a chemical used in rubber production. Consequently, it may be present in rubber as a degradation product.⁶ The most prominent industrial use of carbon disulfide is in the production of viscose rayon fibers. Carbon disulfide is also used in the production of carbon tetrachloride and cellophane, and as a solvent for rubber, sulfur, oils, resins, and waxes.² Carbon disulfide was detected at low concentrations in 4 out of 4 balloon samples in consumer product testing by the Danish EPA.⁷ It was detected in 1 out of 2 natural rubber pacifiers in testing by the Dutch government.⁶

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Substance name Methyl ethyl ketone (also called MEK or 2-butanone)

Toxicity

MEK is listed in Reprotext as a class A- for its potential to be a human reproductive hazard.¹ Evidence is principally based on animal evidence of developmental effects at high doses.²⁻⁵ Some of the animal evidence for MEK comes from studies of 2-butanol which is rapidly converted to MEK in mammals. EPA's oral reference dose for MEK is based on developmental effects seen in a reproductive and developmental toxicity study of 2-butanol in rats.⁶ Human evidence of reproductive and developmental effects is limited and is not specific to MEK as workers were also exposed to other solvents.^{1,6}

Exposure

MEK is a solvent used in various coatings, adhesives, and inks. It is a solvent for nitrocellulose, lacquers, rubber cement, printing inks, paint removers, vinyl films, resins, rosins, polystyrene, chlorinated rubber, polyurethane, acrylic coatings, and cleaning solutions.⁷ MEK was detected in a children's slimy toy and in 3 out of 6 tents in testing by the Danish EPA.⁸ MEK is listed as an ingredient in over 30 arts and crafts products.⁹

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Substance name 1,1,2,2-Tetrachloroethane

Toxicity

1,1,2,2-Tetrachloroethane (1,1,2,2-TCA) is listed as a carcinogen by authoritative sources.^{1,2} Evidence is based on liver cancers in male and female mice and inconclusive information in humans.^{2,3} 1,1,2,2-TCA is also acutely toxic in people and animals; the primary effects are damage to liver and kidney, the nervous system, and blood system.⁴

Exposure

1,1,2,2-TCA was historically used as a solvent and extractant. According to multiple sources, it is no longer widely used for this purpose.^{3,4,5} In Europe, 1,1,2,2-TCA is only used as a feedstock for the production of other chlorinated hydrocarbons. It may also be an incidental byproduct of other production processes for chlorinated hydrocarbons such as the production of vinyl chloride.⁴ Testing of children's products by the Danish EPA detected 1,1,2,2-TCA in 2 out of 2 baby feeding pillow pellets.⁶ It was not detected in a large biomonitoring study of the general U.S. population in 2003-2004.⁷

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Substance name 2,2',6,6'-tetrabromo-4,4'-isopropylidenediphenol (TBBPA)

Toxicity

An oral study in pregnant rats with TBBPA in its formulated product, Saytex 111, reported reduced fetal weight, increased malformations, and fetal death (ICI Americas 1985 study cited in NIEHS¹). Multiple subsequent studies on the technical compound did not show consistent reproductive or developmental toxicity.² Kidney toxicity following oral dosing was reported in newborn rats.³

TBBPA has been shown to compete with thyroid hormone (T4) in binding to transthyretin serum binding protein *in vitro*.^{1,2} It also appears to have potential to act as a thyroid hormone antagonist.^{4,5} TBBPA binds to the estrogen receptor but does not appear to be a receptor agonist or to have significant estrogenic potential.^{2,6} It is not currently listed as an endocrine disruptor by the European Union.

Exposure

This substance is listed as a Persistent, Bioaccumulative and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320).⁷ TBBPA has been detected in breast milk in several small studies of the general population in Europe.^{2,8}

TBBPA is a high production volume (HPV) chemical that is used as both a reactive and additive flame retardant in plastics, adhesives, paper, and textiles.^{1,2} It may constitute up to 22% of ABS polymer resins.² It is used primarily in electrical and electronic equipment. TBBPA is also used as a plasticizer, a component in adhesives and coatings, and a chemical intermediate for the synthesis of other flame retardants (e.g., TBBPA allyl ether).²

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Substance name Bisphenol A

Toxicity

Bisphenol A causes reproductive and developmental toxicity in laboratory animals at high doses.^{1,2,3} At low doses that are similar to estimated exposures in people, bisphenol A can affect the developing rodent brain and behavior, prostate and mammary gland development, and cause early onset of puberty in females.¹ There is wide variability in reported results from studies at low doses.^{1,2,3}

Exposure

Bisphenol A is used to manufacture polycarbonate plastics which are used in many children's toys, dishware, and bottles. BPA is also used in epoxy resins used in food can liners and dental sealants.^{4,5} Consumer product testing by the Danish EPA found BPA in polycarbonate components of pacifiers, in infant baby bottles, and in plastic spoons.⁶ In a large biomonitoring study in the USA, BPA was detected in 92.6% of the general population aged 6 years and older. Children had higher levels than adults. This indicates widespread exposure to children and adults.⁷

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Toxicity

Diethyl phthalate has been classified as a Category 1 endocrine disruptor by the European Union based on reproductive effects.¹ In a multi-generation mouse study, epididymal sperm concentration in second generation offspring of the group treated with diethyl phthalate was reduced by 30 percent compared to controls.² Human studies show an association between increased prenatal urinary concentrations of MEP, the primary urinary metabolite of DEP, and changes in hormone concentrations and anogenital distance in male infants. They also report decreased sperm concentrations and decreased sperm motility associated with higher urinary MEP in adult males.³⁻⁷

Exposure

The Danish EPA found diethyl phthalate in plastic components of baby carriers,⁸ in activity carpet,⁹ and in 4 out of 5 PVC soap containers.¹⁰ Monoethyl phthalate, a metabolite indicative of diethyl phthalate exposure, was found in most of the U.S. population sampled in the NHANES survey.¹¹

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Toxicity

Dibutyl phthalate has been classified as a developmental and a reproductive toxicant by the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction¹ and by the state of California.² The National Toxicology Program concluded that there is clear evidence of developmental and reproductive toxicity.¹ Adverse effects in animals included reduced fetal survival, reduced birth weight, reduced fertility in females, and damage to the developing male reproductive tract.¹ Dibutyl phthalate has been classified as a Category 1 endocrine disruptor by the European.³

Exposure

The Danish EPA found dibutyl phthalate in numerous children's products including clothing (infant), foam toys, a fluorescent light stick, school supplies, and coatings on wood toys.⁴ A Dutch study found dibutyl phthalate in a wide range of plastics in children's products.⁵ Mono-n-butyl phthalate, a metabolite indicative of dibutyl phthalate exposure, was found in >99 percent of the U.S. population sampled in the NHANES survey.⁶

References

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CAS 84-75-3

Substance name Di-n-Hexyl Phthalate

Toxicity

Di-n-hexyl phthalate is considered a reproductive toxicant by the state of California and the National Toxicology Program.^{1,2} Di-n-hexyl phthalate reduced fertility in both male and female rodents, reduced survival of offspring after birth, and caused severe degenerative changes in the seminiferous epithelium of male rats.^{1,2} There is also evidence that exposure *in utero* can damage the male reproductive system, cause fetal growth retardation, malformations, and fetal loss.^{1,3}

Exposure

Di-n-Hexyl phthalate is mainly a component of other phthalates. Phthalates are used primarily as plasticizers to add flexibility to plastics. Available information indicates that DnHP is manufactured in relatively small amounts but occurs in industrially important phthalates such as diisohexyl phthalate (up to 25%).¹ Commercial phthalate substances containing DnHP may be added to the polyvinyl chloride (PVC) utilised in the manufacture of notebook covers, toys, and shoes.^{1,4} We did not locate biomonitoring data nor could we find testing results that reported its presence in children's products.

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CAS 85-44-9

Substance name Phthalic anhydride

Toxicity

In animal studies, phthalic anhydride had effects on rodent lung and kidneys and on fetal development at high doses.^{1,2} There is also limited evidence of adverse effects on sperm in laboratory mice.^{3,4} In workplace settings, inhalation and dermal exposures have been associated with irritation and allergic sensitization.^{4,5}

Exposure

Phthalic anhydride is primarily used in the manufacture of phthalate plasticizers and polyester resins. It is also used in small volume in the production of alkyl resins used in dyes, paints, and lacquers.^{4,6} It was detected by the Danish EPA in coatings on 4 out of 15 wooden toys tested.⁷ Phthalic anhydride was not listed as a direct ingredient in any product in the NLM database.⁸

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CAS 85-68-7

Substance name Butyl benzyl phthalate (BBP)

Toxicity

Butylbenzyl phthalate has been classified as a developmental and a reproductive toxicant by the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction¹ and by the state of California.² The National Toxicology Program concluded that there is clear evidence of developmental toxicity and some evidence of male reproductive toxicity.¹ Effects in animals included reduced sperm counts, reduced male fertility, prenatal mortality, and skeletal, visceral, and external malformations.¹ Butylbenzyl phthalate has been classified as a Category 1 endocrine disruptor by the European Union.³

Exposure

The Danish EPA found butylbenzyl phthalate in the coating of a wood toy.⁴ A Dutch study of plastics in children's products found butylbenzyl phthalate in 2 out of 7 polyurethane plastics.⁵ Mono-benzyl phthalate, a metabolite indicative of butylbenzyl phthalate exposure, was found in >98 percent of the U.S. population sampled in the NHANES survey.⁶

References

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CAS 86-30-6

Substance name N-Nitrosodiphenylamine

Toxicity

N-nitrosodiphenylamine is considered a carcinogen by two authoritative sources.^{1,2} In laboratory animals it causes bladder tumors, and reticulum cell sarcomas. It is structurally similar to other carcinogenic nitrosamines.^{1,2}

Exposure

N-nitrosodiphenylamine has been used as an additive in the manufacturing process for vehicle tires and some other rubber products.³ Use and production has declined since the 1970s as it was replaced by other chemicals.³ The Danish EPA found N-nitrosodiphenylamine in one out of 4 balloons tested.⁴

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CAS 87-68-3

Substance name Hexachlorobutadiene (HCDB)

Toxicity

Hexachlorobutadiene is classified as a possible human carcinogen by the U.S. EPA.¹ HCBD is genotoxic in mammalian cell cultures and binds with DNA in rats and mice *in vivo*.² Studies in animals show a selective adverse effect of HCBD on the kidney, specifically the proximal tubule.^{3,4} HCDB accumulates in brain tissue and is neurotoxic in animal studies.^{3,4} HCBD caused reproductive and developmental effects at oral doses that were neurotoxic and damaged the kidney of the mothers.⁴

Exposure

This substance is listed as a Persistent, Bioaccumulative and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320).⁵ HCBD is used as an industrial solvent and chemical intermediate in the manufacture of rubber compounds, chlorofluorocarbons, and lubricants. It is also formed as a byproduct during the manufacture of some chlorinated compounds.² It has been widely detected in ambient air, water, foods and human tissues.⁶

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Propyl paraben	(CAS 94-13-3)
Butyl paraben	(CAS 94-26-8)
Methyl paraben	(CAS 99-76-3)
Ethyl paraben	(CAS 120-47-8)
<i>para</i> -Hydroxybenzoic acid	(CAS 99-96-7)

Due to similarities in use, exposure, and toxicity; the parabens are grouped in one summary.

Summary

These five chemicals meet the Department of Ecology's criteria for inclusion on the CHCC list. There is widespread exposure to parabens and *p*-hydroxybenzoic acid (PHBA) in the U.S., and because of evidence of endocrine disruption, it is important to collect more information about the use of these chemicals in children's products. Although there were both positive and negative studies for many potentially harmful effects, the weight of evidence indicates that these chemicals have estrogenic activity, can interfere with normal sperm development, and can alter testosterone levels. Several parties contend that parabens are safe at the levels used in products, but there is some debate about the margin of safety. While toxicity studies have focused on the effects of individual compounds, children's products often contain mixtures of two or more parabens. The parabens and *p*-hydroxybenzoic acid are structurally related compounds that often appear to have similar biological activities in experimental studies, and it is therefore important to consider the potential for additive or synergistic effects from exposure to mixtures of these chemicals.

Toxicity

All five chemicals have been classified as Category 1 endocrine disruptors by the European Union.¹

Estrogenic effects: All the widely used parabens have been shown to possess estrogenic activity to different extents in different assay systems *in vitro* and *in vivo*. Twenty four out of twenty five *in vitro* studies of estrogenic effects reported positive findings for parabens.² The estrogenic effects of treatment with multiple parabens appear to be additive.³ The estrogenic activity of parabens is known to increase with increasing chain length and with branching of the alkyl chain. Estrogenic activity of PHBA has been demonstrated in several assays.²

In uterotrophic assays, all four parabens and PHBA showed estrogenic activity in at least one *in vivo* study, while at least one other study showed negative results for each compound.² The lowest NOAELS and LOAELS are shown in the Table 1 below.²

Table 1

Compound	NOAEL (mg/kg bw)	LOAEL (mg/kg bw)
Methyl paraben	5.5	16.5
Ethyl paraben	6	18
Propyl paraben	6.5	20
Butyl paraben	0.7	7
PHBA	0.5	5

Parabens generally have lower binding affinity to estrogen receptors than some other estrogenic ligands (such as 17 β -estradiol or DES), and parabens are often termed “weak estrogens”. The estrogenic potentials of parabens have been studied in estrogen receptor (ER) α competitive binding assays, as well as studies that examined other aspects of estrogenicity including ligand ability to regulate an estrogen-responsive gene (ERE-CAT) transfected into MCF-7 cells, and ligand ability to regulate estrogen-dependent proliferation of MCF-7 cells. In the competitive binding assay, all parabens studied were at least 10,000 to 100,000 times less potent than 17 β -estradiol.⁴ In MCF-7 cells with a stably transfected estrogen-regulated ERE-CAT reporter gene, the tested parabens showed effects similar to 17 β -estradiol, although at 1000–10,000 times greater concentrations. Depending on the endpoint measured and the specific paraben under study, these compounds are from 1000 to 1,000,000 times less potent than 17 β -estradiol.⁴

However, with sufficient concentrations, the parabens gave responses in whole cell assays in terms of increased gene expression and cell proliferation in human breast cancer cells of the same magnitude as 17 α -estradiol. This shows that parabens are not partial agonists, as might be implied by the term ‘weak’, but give full agonist responses in whole cells at sufficiently high concentrations. There is some indication that blood levels of parabens and their metabolites are significantly higher than levels of natural estradiol and therefore, despite their lower binding affinity, could interfere with normal functioning of processes regulated by estrogens.²

Effects on males: Studies in young male rats have shown adverse effects on sperm production and testosterone levels following oral exposure to parabens with longer side chains, specifically butyl paraben and propyl paraben.

Propyl paraben (8 weeks of dietary exposure) reduced daily sperm production at all doses tested (10 mg/kg, 100 mg/kg, and 1000 mg/kg). Similarly, serum testosterone levels were reduced at all three dose levels, but the effect was statistically significant only at 1000 mg/kg.⁵

Butyl paraben reduced daily sperm production (testis sperm counts) as well as epididymal cauda sperm counts in a dose-related manner in all applied doses of approximately 10, 100 and 1000 mg/kg bw/day. Serum testosterone was reduced at 100 and 1000 mg/kg bw/day showing a dose-response relationship. Relative epididymis weight was reduced at 100 and 1000 mg/kg bw/day with a dose-response

relationship.^{6,7} These results suggest a LOAEL of 10 mg/kg bw/day and no identifiable NOAEL for propyl paraben and butyl paraben.

Hoberman et al.⁸ performed a repeat of the 2001 study by Oishi⁶ by exposing young male rats in the diet to 10, 100 and 1000 mg/kg bw/day of butylparaben. This study was performed under Good Laboratory Practices conditions and included a higher number of animals than the Oishi study. The authors reported “no adverse effects” at all dose levels concluding a NOAEL of 1000 mg/kg bw/day. However, serum testosterone was reduced significantly after 3 weeks of dosing at 100 and 1000 mg/kg bw/day.

In a study of methyl paraben, Hoberman et al. reported statistically significant increases in the number of abnormal sperm in the two highest dose groups (100 mg/kg and 1000 mg/kg), and the testicular spermatid concentration appeared dose-dependently decreased (to 77% of control level), although this was not statistically significant.⁸

Recent reports have documented that several parabens have the ability to bind to the androgen receptor and anti-androgenic activity was found for all the parabens tested. Additionally, in a recent *in vitro* study, methyl-, propyl- and butyl-4-hydroxybenzoate were shown to be androgen receptor antagonists, and some of the parabens could inhibit testosterone induced transcriptional activity by as much as 40% at a concentration of 10 μ M.⁹

Exposure

Parabens are the most widely used preservatives in cosmetic products.¹⁰ Various parabens and paraben mixtures are intentionally added to thousands of cosmetic products. Methyl paraben and propyl paraben have been Generally Recognized As Safe by the FDA for direct addition to foods at levels <0.1%. Para-hydroxybenzoic (PHBA) acid is a precursor used in the manufacture of parabens and is also a common metabolite in humans following oral or dermal exposure to parabens.

Parabens are used in many children’s products.

The Danish EPA identified methyl paraben as a listed ingredient in 95 of 208 children's personal care products, 7 of 28 sunscreens, and 7 of 32 lotions in studies of cosmetics marketed for children.^{11,12} Methyl paraben was also found in 2 of 26 marker pen sets,¹³ 1 of 3 gel pens,¹³ and several slime toys.^{14,15} A Dutch study of plastics in children’s products found methyl paraben in 1 out of 18 samples of ethylene vinyl acetate plastic.¹⁶

The Danish EPA identified ethyl paraben as a listed ingredient in 46 of 208 children's personal care products, 2 of 28 sunscreens, and 4 of 32 lotions in studies of cosmetics marketed for children.^{11,12} Ethyl paraben was found in 1 of 14 slime toys.¹⁴

The Danish EPA identified propyl paraben as a listed ingredient in 70 of 208 children's personal care products, 5 of 28 sunscreens, and 6 of 32 lotions in studies of cosmetics marketed for children.^{11,12} Propyl paraben was found in 3 of 14 slime toys.¹⁴

The Danish EPA identified butyl paraben as a listed ingredient in 48 of 208 children's personal care products, 1 of 28 sunscreens, and 1 of 32 lotions in studies of cosmetics marketed for children.^{11,12} Butyl paraben was found in 1 of 14 slime toys.¹⁴

The Danish EPA found para-hydroxybenzoic acid in 1 slime toy.¹⁵ A Dutch study of plastics in children's products found para-hydroxybenzoic acid in 2 out of 18 samples of ethylene vinyl acetate plastic.¹⁶

Analysis for parabens in urine of the general U.S. population was conducted in the NHANES survey during 2005 – 2006; and two or more were detected in almost all people sampled.¹⁷ Table 2 below shows percent detection for four parabens.

Table 2

Compound	Percentage detected
Methyl paraben	99.1%
Ethyl paraben	42.4%
Propyl paraben	92.7%
Butyl paraben	47.0%

For some children 6 to 11 years old, urinary excretion exceeded one milligram per day (Table 3).¹⁷

Table 3

Compound	Urinary Excretion 50 th percentile (µg/L)	Urinary Excretion 95 th percentile (µg/L)
Methyl paraben	25	1560
Ethyl paraben	Not detected	9.9
Propyl paraben	2.5	125
Butyl paraben	Not detected	7.5

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CAS 95-53-4

Substance name 2-Aminotoluene (also called *ortho*-toluidine)

Toxicity

2-Aminotoluene is classified as a carcinogen by authoritative sources.¹⁻⁴ Animal evidence includes bladder and liver cancers as well as tumors in various tissues. Studies of exposed workers have reported that 2-aminotoluene and 2-aminotoluene hydrochloride exposure are associated with increased bladder cancer in humans. Definitive conclusions are limited by the fact that workers were almost always exposed to multiple chemicals including other possible bladder carcinogens.^{1,2}

Exposure

2-Aminotoluene and its hydrochloride salt are primarily used as chemical intermediates in making over 90 dyes and pigments. They are used in acid-fast dyestuffs, azo pigment dyes, sulfur dyes, indigo compounds, and optical brighteners. 2-Aminotoluene is also used as an intermediate for synthetic rubber and rubber vulcanizing chemicals, pharmaceuticals, and pesticides.^{1,2,5} Studies by the Danish EPA detected this compound in 1 out of 4 balloon samples, in infant mittens, and in wool fabric. The source of residues may be synthetic rubber and dyes used in fabrics.⁶

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CAS 95-80-7

Substance name 2,4-Diaminotoluene

Toxicity

2,4-Diaminotoluene is classified as a carcinogen by authoritative sources.¹⁻⁴ Evidence is based on liver and mammary gland tumors in rats and mice. The European Union considers it a genotoxic carcinogen.³ Oral studies in rodents have also shown adverse effects on the male reproductive tissues including testicular atrophy, altered levels of male hormones, and depression in spermatogenesis.³

Exposure

2,4-Diaminotoluene is used in the production of toluene diisocyanate which is used to make polyurethane. It is or has been used in the production of dyes used to color paper, fur, leather, and textile fabrics.^{2,3} 2,4-Diaminotoluene was detected in a children's doll fabric in testing of textile toys by the Dutch Government.⁵

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CAS 100-41-4

Substance name Ethylbenzene

Toxicity

Ethylbenzene is classified as a carcinogen by authoritative sources.^{1,2,3} Evidence is based on liver and kidney toxicity in rodents, kidney tumors in rats, and lung and liver tumors in mice.⁴ Ethylbenzene can produce developmental effects in rabbits, mice, and rats although these effects may be secondary to maternal toxicity.⁴

Exposure

Ethylbenzene is a high production chemical used primarily in the production of styrene monomer, with smaller amounts used to make several other chemicals.⁴ Ethylbenzene is present at up to 25% in mixed xylenes which are used as solvents in many products.³ Ethylbenzene was detected in consumer product testing by the Danish EPA in marker pens, slimy toys, and children's tents.⁵ It was also listed on the MSDS of lacquer applied to wooden toys at 1-2.5%.⁵ Ethylbenzene was detected widely in the blood of the general U.S. population.⁶

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Toxicity

Styrene is listed as a carcinogen by IARC based on limited evidence of lymphatic and hematopoietic cancer in occupationally exposed people and limited evidence of cancer in animals.¹ Styrene appears to produce developmental effects in laboratory animals but the effects may be secondary to maternal toxicity.² Developmental effects reported include reduced growth and survival and alterations in neurochemicals.^{1,2} Central and peripheral nervous system effects have also been reported in exposed workers.¹

Exposure

Styrene is a high production chemical used to manufacture polystyrene resins. It is also used as a copolymer with acrylonitrile and 1,3-butadiene in ABS plastic and with butadiene in SBR synthetic rubber.² Polystyrene resins are readily molded and are used extensively in the fabrication of plastic packaging, disposable beverage tumblers, and toys.¹ In consumer product testing by the Danish EPA, styrene was detected in slimy toys, children's tents, nursing and baby feeding pillows, baby mattress covers, children's bed linens, infant jackets, and infant mittens.³ Biomonitoring of the general U.S. population detected styrene in less than half of the population.⁴

Resources

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CAS 104-40-5

Substance name 4-Nonylphenol; 4-NP

Toxicity

4-nonylphenol has been classified as a Category 1 endocrine disruptor by the European Union.¹ Uterotrophic assays indicate that nonylphenol has estrogenic activity.²⁻⁴

Exposure

The Danish EPA found 4-nonylphenol in 1 out of 2 nursing pillows.⁵ 4-nonylphenol was found in a variety of plastics in a Dutch survey of plastic children's toys.⁶ In a large biomonitoring study of the general U.S. population, 51% of people had 4-nonylphenol in their urine.⁷

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CAS 106-47-8

Substance name *para*-Chloroaniline

Toxicity

para-Chloroaniline is classified as a carcinogen by authoritative sources.¹⁻³ Evidence is based primarily on cancers in the spleen and liver of test animals.¹ Both animal and human occupational exposures have resulted in methemoglobinemia, a blood disorder that results in hypoxia. Infants have also suffered from methemoglobinemia when chlorohexidine, which decomposes spontaneously to *para*-chloroaniline, was used in their hospital incubators.^{1,4}

Exposure

para-Chloroaniline has been used in the manufacture of dyes and pigments and as a chemical intermediate in the production of other chemicals.^{1,4} The general public may be exposed to *para*-chloroaniline through dyed textiles, printed papers, cosmetics, and pharmaceutical products.⁴ Testing on consumer products by the Danish EPA found the chemical in acrylic paints for children and dyed fabric on a stuffed bear.⁵

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Substance name Acrylonitrile

Toxicity

Acrylonitrile is classified as a carcinogen by authoritative sources.¹⁻⁵ Long term studies in laboratory animals have shown cancers of the digestive tract, mammary gland, and the central nervous system.^{2,4} Occupational studies have shown excesses of lung and prostate cancers as well as other sites in humans.²

Exposure

Acrylonitrile is an important industrial chemical intermediate. It is used extensively in the manufacture of synthetic fibers (e.g. acrylic fibers). It is also used in copolymer plastics (e.g., ABS and SAN) for a variety of consumer goods such as dinnerware, food containers, toys, luggage, and small appliances.^{2,4} It is used in the manufacture of children's products but we were unable to locate any testing data for end use products covered by CSPA.

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CAS 107-21-1

Substance name Ethylene glycol

Toxicity

Ethylene glycol causes fetal death and malformations when fed to rodents during pregnancy.^{1,2} The National Toxicology Program concluded that “ethylene glycol may adversely affect human development if oral exposures are sufficiently high.”¹

Exposure

Ethylene glycol lowers the freezing point of water. It is used in antifreeze, in aircraft deicing fluids, and in condensers and heat exchangers. It is a chemical intermediate in the production of polyester compounds.^{1,3} It has also been used as a glycerin substitute in commercial products such as paints, lacquers, detergents, and cosmetics.³

In two online databases ethylene glycol is listed as an ingredient in a diaper ointment⁴ and in body wash/cleansers, acne treatment, athlete's foot treatment, hair color, hair conditioners, and a home hair perm kit.⁵ Product testing for the Danish EPA detected ethylene glycol in balloons and tents.⁶

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CAS 108-88-3

Substance name Toluene

Toxicity

Toluene is a known neurotoxicant and is listed as a developmental toxicant by the state of California.¹ Studies in laboratory animals indicate that gestational exposure can induce alterations in brain development and result in low birth weight.² Studies of human babies born to mothers who abused solvents during pregnancy (e.g., glue sniffers) have reported similar effects: perinatal death, preterm delivery, small brain size at birth, low birth weight, and neurodevelopmental delays.^{3,4}

Exposure

Toluene is a high production chemical that is widely used as a solvent in paints, coatings, adhesives, inks, and cleaning agents.^{4,5} It is used in the production of other chemicals such as benzene.³ Toluene is also used in production of polymers to make nylon, plastic soda bottles, and polyurethanes; and in some pharmaceuticals, and dyes.⁵ Toluene is listed as an ingredient in hundreds of paints, sealers, strippers, autoshop and cleaning items⁶ but few of these products would be marketed to children. Some hobby glues and liquid nails with toluene might be used by children. Toluene was detected in a wide variety of children's products in consumer product testing by the Danish EPA. It was detected in 1 of 5 infant jackets, 2 of 4 infant mittens, 2 of 3 school erasers, 1 or 4 pencil cases, 6 of 6 tents, 14 of 14 slimy toys, and 2 of 15 wooden toys. It was also reported in hobby adhesives.⁷

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CAS 108-95-2

Substance name Phenol

Toxicity

High levels of oral or inhalation exposure during pregnancy resulted in dose-dependent fetotoxicity in animals studies.^{1,2,3} The EPA oral reference dose is based on a developmental toxicity study in rats which showed decreased fetal body weight and delayed ossification of bones.⁴ Phenolic disinfectants in hospital neonatal units have caused outbreaks of hyperbilirubinemia in infants and some cases of fetal death.⁵

Exposure

Phenol was found in various children's products in testing by the Danish EPA.⁶ it was detected in a nursing pillow, a balloon, glitter glue, an infant jacket, in ABS and PVC plastics, a tent, and a coating on a wooden toy. Phenol is also listed as an ingredient in diaper rash ointment, lip products, and dandruff shampoo in an online database of personal care products.⁷

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CAS 109-86-4

Substance name 2-Methoxyethanol (also called ethylene glycol monomethyl ether)

Toxicity

2-Methoxyethanol is listed as a reproductive hazard by the state of California and the European Union.^{1,2} It causes reproductive and developmental toxicity in laboratory animals including reduced fertility, effects on sperm and male gonads, fetotoxicity, and low birthweights.³⁻⁶ Cases of occupational exposures associated with testicular effects have been reported.⁴ Hematotoxic effects have also been reported.^{4,5}

Exposure

2-Methoxyethanol has been used as a solvent for low viscosity cellulose acetate, varnishes, dyes, and resins. It may also be used in paper board manufacturing.⁴ The Danish EPA tested coatings on wooden toys and found it in 1 of the 15 coatings tested.⁷

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CAS 110-80-5

Substance name Ethylene glycol monoethyl ether (also called 2-ethoxyethanol)

Toxicity

Ethylene glycol monoethyl ether is listed as a reproductive hazard by the state of California and the European Union.^{1,2} Consistent adverse effects on male reproductive organs and sperm have been observed in multiple species. These effects include testicular atrophy, degeneration of testicular tubules, decrease in sperm counts and motility, and an increase in the number of abnormal sperm cells.³ Ethylene glycol monoethyl ether has been shown to affect fertility in both sexes of rodents and cause developmental effects.³ Hematotoxic effects, such as hemolytic anemia, have also been reported.³

Exposure

Ethylene glycol monoethyl ether is primarily used as a chemical intermediate in the chemical industry. It is also used as an industrial solvent for nitrocellulose, varnish removers, cleansing solutions, and dye baths. It has been used for the formulation of paints, lacquers, varnishes and printing inks.^{3,4} Its use as a solvent in cleaning agents and cosmetics may have been phased out in Europe due to concerns about reproductive toxicity.³ Testing by the Danish EPA found it in marker pen sets, the coatings of wooden toys, and children's tents.⁵

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http://www.mst.dk/English/Chemicals/Consumer_Products/Surveys-on-chemicals-in-consumer-products.htm

CAS 115-96-8

Substance name Tris (2-chloroethyl) phosphate (TCEP)

Toxicity

Tris(2-chloroethyl) phosphate is classified as a carcinogen by the state of California and a reproductive hazard by the European Union.^{1,2} TCEP caused kidney tumors and cancers in rats and mice in studies conducted by the National Toxicology Program.³ In studies reviewed by the European Union, TCEP caused significant impairment of fertility and adverse effects in male reproductive organs and sperm parameters.²

Exposure

TCEP has been used as an additive plasticizer and viscosity regulator with flame-retarding properties for polyesters, polyurethane, polyvinyl chloride and other polymers.⁴ TCEP can be released from items treated with TCEP flame retardant such as foam rubber, carpets, and plastic materials as a result of abrasion.² TCEP was detected in the foam and covering fabric of a foam play cube in testing of toys by the Danish EPA.⁵ In a study by the Netherlands Government, TCEP was detected in ethylene vinyl acetate and polyurethane plastics in toys that are likely to be sucked by children under two years old.⁶ TCEP production and use have reportedly declined since other flame retardants were adopted for rigid and flexible polyurethane foams.²

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Substance name Di-2-ethylhexyl Phthalate

Toxicity

Di-2-ethylhexyl phthalate (DEHP) has been listed as a carcinogen by authoritative sources.^{1,2,3} It has been found to cause hepatocellular carcinomas in laboratory animals.^{1,2} DEHP has been classified as a developmental and a reproductive toxicant by National Toxicology Program Center for the Evaluation of Risks to Human Reproduction and the state of California.^{3,4} The National Toxicology Program concluded that there is clear evidence it can cause developmental and reproductive toxicity in laboratory animals.⁴ Effects included skeletal and cardiovascular malformations, neural tube defects, developmental delays, intrauterine death and adverse effects on the male and female reproductive tract.⁴ DEHP has been classified as a Category 1 endocrine disruptor by the European Union.⁵

Exposure

The Danish EPA found di-2-ethylhexyl phthalate in numerous children's products including clothing (infant), foam toys, pacifiers, school supplies, slimy toys, packaging for cosmetics, a perambulator cover, and the coatings on a wood toy.⁶ Dutch studies found it in a wide range of plastics in children's products⁷ and in a baby feeding spoon.⁸ Several metabolites indicative of di-2-ethylhexyl phthalate exposure were found in the population sampled for the NHANES survey, indicating that >98 percent of the U.S. population is exposed to DEHP.⁹

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CAS 117-84-0

Substance name Di-n-octyl phthalate

Toxicity

The National Toxicology Program found limited evidence that di-n-octyl phthalate caused adverse developmental effects in laboratory animals.¹ Multiple animal studies have demonstrated that di-n-octyl phthalate can be toxic to the liver, kidney, thyroid, and immune system.²

Exposure

Di-n-octyl phthalate is a common plasticiser in plastic production.² The Danish EPA found di-n-octyl phthalate in several children's products including foam toys, PVC soap containers, packaging for cosmetics, and a set of marker pens.³ A Dutch study found di-n-octyl phthalate in several plastics in children's products.⁴ Mono-(3-carboxypropyl) phthalate, a metabolite indicative of di-n-octyl phthalate exposure, was found in >60 percent of the U.S. population sampled in the NHANES survey.⁵

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CAS 118-74-1

Substance name Hexachlorobenzene (HCB)

Toxicity

Hexachlorobenzene is classified as a carcinogen by authoritative sources.¹⁻⁴ HCB causes liver tumors in laboratory animals. HCB is listed as developmental toxicant by the state of California primarily based on altered neurobehavioral development in offspring of dosed rodents.^{5,6} HCB has been shown to induce structural and functional changes in primate ovaries⁶ and is listed as a Category 1 endocrine disruptor by the European Union.⁴

Exposure

Hexachlorobenzene is listed as a Persistent, Bioaccumulative and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320).⁷ No current U.S. commercial uses of hexachlorobenzene were identified but HCB is formed as a by-product or impurity in the manufacture of other chlorinated chemicals.² The FDA, Cosmetics Office detected HCB in U.S.-certified color additives. Their analysis suggested that the contamination with HCB may be decreased by avoiding use of starting material (tetrachlorophthalic anhydride) heavily contaminated with HCB.⁸ Biomonitoring shows widespread but declining detections in the U.S. general population.⁹

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CAS 119-93-7

Substance name 3,3'-Dimethylbenzidine (also called *ortho*-Tolidine)

Toxicity

3,3'-Dimethylbenzidine and dyes metabolized to 3,3'-dimethylbenzidine are listed as carcinogens by authoritative sources.¹⁻⁴ Evidence is based on cancer of the skin, liver, oral cavity, intestinal tract, lung, and mammary gland observed in test animals.^{2,5}

Exposure

3,3'-Dimethylbenzidine has been used as a dye or an intermediate for producing a large number of dyestuffs and pigments.² These dyes have been used to color leather, textiles, and paper.⁶ 3,3'-Dimethylbenzidine is also used in the production of polyurethane-based elastomers, coatings, and rigid plastics.⁶ Danish EPA testing of hobby products marketed to children found it in a gel pen.⁷

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CAS 123-91-1

Substance name 1,4-Dioxane

Toxicity

1,4-Dioxane is classified as a carcinogen by authoritative sources.¹⁻⁴ Evidence is based on liver tumors in multiple animal species as well as tumors at other sites.^{1,3} There is some evidence that 1,4-dioxane acts as a tumor promoter.^{1,3} 1,4 dioxane has also caused liver and kidney toxicity in laboratory animals and in people who were occupationally exposed.¹

Exposure

1,4-Dioxane is primarily used as a solvent for chemical processing. It is used in the manufacturing of products such as adhesives, cleaning and detergent preparations, cosmetics, deodorant fumigants, emulsions and polishing compositions). It is unintentionally formed as an impurity during the manufacture of alkyl ether sulfates and other ethoxylated substances which are used in consumer products such as cosmetics, detergents, and shampoos.⁶ Testing in the Europe detected 1,4-dioxane in baby lotion, in shampoos and lotions, and in hand dishwashing liquids.⁵ The U.S. FDA has detected 1,4-dioxane in ethoxylated raw materials for cosmetics and in finished cosmetic products including baby shampoos and bubble baths.⁶

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Substance name Perchloroethylene (also called tetrachlorethene or tetrachloroethylene)

Toxicity

Perchloroethylene is a halogenated hydrocarbon classified as a carcinogen by authoritative sources.¹⁻³ Evidence from laboratory animals shows it can cause liver cancer and leukemia in rodents.^{1,2} Human evidence comes from studies of people occupationally exposed to perchloroethylene either through manufacturing or dry cleaning. The most consistent evidence across these studies suggests there may be an association between increased exposure and increased incidence of esophageal and cervical cancer and non-Hodgkin's lymphoma.² Conclusions are limited by co-exposures to petroleum solvents and other dry cleaning agents.²

Exposure

Perchloroethylene is a high production volume chemical used in dry cleaning garments, metal cleaning and synthesis of other chemicals.⁴ It is used in the textile industry for cleaning, processing, and finishing.¹ It has been used in household products like spot removers, lubricants, and water repellents.⁴ Consumer product testing by the Danish EPA detected it in children's tents but not in a study of textiles.⁵ Biomonitoring of the general U.S. population detected perchloroethylene in about one quarter of the people tested in 2001-02.⁴

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CAS 131-55-5

Substance name Benzophenone-2 (also called 2,2,4,4-tetrahydroxybenzophenone)

Toxicity

Benzophenone-2 has been classified as a Category 1 endocrine disruptor by the European Union.¹ It has shown estrogenic activity in rat uterotrophic assays². Studies in mice³ and rats⁴ demonstrated dose dependent estrogenic effects.

Exposure

The Danish EPA identified benzophenone-2 as a listed ingredient in 2 of 208 children's personal care products in the mapping study of cosmetics marketed to children.⁵

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CAS 140-66-9

Substance name 4-tert-Octylphenol (also called 4-(1,1,3,3-tetramethylbutyl)phenol)

Toxicity

4-tert-octylphenol has been classified as a Category 1 endocrine disruptor by the European Union.¹ Studies in rats have found 4-tert-octylphenol to have uterotrophic effects,² to cause early vaginal opening,³ to disrupt the estrous cycle,⁴ and to cause abnormal sperm development.⁵

Exposure

A Dutch study of plastics in children's products found 4-tert-octylphenol in 5 out of 48 polyvinyl chloride plastics and 1 poly(isopropyl methacrylate) plastic.⁶ In a large biomonitoring study, 4-tert-octylphenol was detected in 57% of the general US population.⁷

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Substance name Estragole

Toxicity

Estragole is listed as a carcinogen for the state of California.¹ Estragole has been shown to cause liver cancer and organ toxicity in rodents.^{1,2} In its determinations, California also considered that estragole was genotoxic in several short-term tests, caused DNA adduct formation *in vivo* and *in vitro*, was structurally similar to recognized carcinogens, and had a well characterized carcinogenic mode of action that is expected to occur in humans.¹

Exposure

Estragole occurs naturally in many culinary herbs such as anise and basil. It is used as an additive, fragrance, and flavoring agent in cosmetics, cleaning products, and food.^{1,2} In a survey by the Danish EPA, essential oils and fragrances reported estragole on their Material Safety Data Sheets (MSDS) at over 50% estragole in basil oil, and at lower amounts in anise seed star oil, and fennel oil.³

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CAS 149-57-5

Substance name 2-Ethylhexanoic Acid (2-EHA)

Toxicity

2-Ethylhexanoic acid is listed as a developmental toxicant by the state of California and a reproductive and developmental toxicant by the European Union.^{1,2} The National Toxicology Program Center for the Evaluation of Risks to Human Reproduction also reviewed studies of 2-EHA as part of their evaluation of DEHP.³ It concluded that there was sufficient animal evidence to identify 2-EHA as a developmental toxicant.^{3,4}

Exposure

Metal derivatives of 2-ethylhexanoic acid are widely used as stabilizers for polyvinyl chloride (PVC). Testing by the Danish EPA found 2-EHA in foam washcloths for babies, baby foam mattresses, nursing pillows, marker pen sets, and a coating on a wooden toy.⁵ Testing by the Dutch government showed frequent detections of 2-EHA migrating out of PVC plastic.⁶

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CAS 556-67-2

Substance name Octamethylcyclotetrasiloxane

Toxicity

Octamethylcyclotetrasiloxane has been classified as a Category 1 endocrine disruptor by the European Union.¹ Octamethylcyclotetrasiloxane demonstrated estrogenic activity in rat uterotrophic assays^{2,3} and in mice.⁴

Exposure

The Danish EPA identified octamethylcyclotetrasiloxane as a listed ingredient in 1 out of 28 sunscreens, 1 of 32 lotions, and 1 out of 208 cosmetics marketed to children.⁵

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CAS 608-93-5

Substance name Pentachlorobenzene

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Toxicity

Pentachlorobenzene has been classified as a Category 1 endocrine disruptor by the European Union.¹ In rats, levels of thyroid hormones (T3 and T4) in plasma were decreased after intraperitoneal injection or dietary ingestion of pentachlorobenzene.^{2,3}

Exposure

Pentachlorobenzene is on the Washington state list of PBTs as being persistent, bioaccumulative and toxic (WAC 173-333-310).⁴ Evidence that pentachlorobenzene is found in children's products was not located. Its use as a fungicide and as a flame retardant were cancelled in U.S. by the early 1980s. The fungicide PCNB (of which pentachlorobenzene is an impurity and a metabolite), was cancelled by the U.S. EPA for residential, school, and golf course uses in 2009.⁵ PCNB is still used agriculturally.

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CAS 842-07-9

Substance name C.I. Solvent Yellow 14

Toxicity

C.I. Solvent Yellow 14 is listed as a carcinogen by the state of California.¹ The listing is based on evidence of dose-related liver cancer in rats but not mice.² Other studies indicate that C.I. Solvent Yellow 14 is genotoxic and that human metabolism would likely activate this chemical to form adducts with DNA.^{3,4}

Exposure

C.I. Solvent Yellow 14 is an azo dye and is used to color waxes, oils, solvents, polishes, cellulose ether varnishes and styrene resins.^{5,6} It was used as a food dye, called Sudan 1, and was common in certain curry and chili powders. The use of Sudan I in foods is now banned in many countries due to reports on its possible health risks.⁶ The Dutch government detected C.I. Solvent Yellow 14 in two plastic samples from toys likely to be sucked by children under 2 years old.⁷

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CAS 872-50-4

Substance name 1-Methyl-2-pyrrolidinon (also called N-methylpyrrolidone or NMP)

Toxicity

N-Methylpyrrolidone is listed by the state of California and the European Union as a developmental toxicant.^{1,2} In animal studies it caused reduced fetal and birth weights, developmental delays and impairment of cognitive skills in offspring.^{1,3,4}

Exposure

1-Methyl-2-pyrrolidinon is used as an industrial solvent for resins, paint strippers, and plastics in the semiconductor industry. It is also used as a finishing agent in textiles, as a pigment dispersant, and as a spinning agent for polyvinyl chloride.^{1,3,5} It is listed as an ingredient under the synonym (methyl pyrrolidone) in a nail polish remover and five mascaras in an online cosmetic database.⁶ The Danish EPA detected 1-methyl-2-pyrrolidinon in the coatings of children's wooden toys.⁷

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CAS 1163-19-5

Substance name 2,2',3,3',4,4',5,5',6,6'-Decabromodiphenyl ether (also known as BDE-209)

Toxicity

BDE -209 is the primary congener found in Deca-BDE. Thyroid and liver appear to be the most sensitive tissues to toxicity of Deca-BDE in animal studies. In 2008, EPA determined that Deca-BDE had “suggestive evidence of carcinogenic potential” in humans.¹ This is based on liver tumors in rats and male mice, and thyroid gland follicular cell hyperplasia and thyroid tumors in male mice in oral studies with Deca-BDE.^{1,2} Rats and mice exposed to Deca-BDE in their early postnatal period, were observed to have neurodevelopmental effects as they matured.^{3,4,5,6} In the environment, BDE-209 is likely to degrade into less-brominated, more toxic BDEs.⁷

Exposure

Deca BDE is listed as a Persistent, Bioaccumulative and Toxic (PBT) chemical under Washington State’s PBT rule (WAC 173-333-320).⁷ This chemical is widely used as a flame retardant in high impact polystyrene and other polymers, in coatings and adhesive systems such as the back coatings for carpets, and in non-clothing textiles.^{1,7} It is a high production volume chemical that has not been reported directly in children’s products but has been found in indoor air and dust and in biomonitoring studies.^{1,7,8,9}

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CAS 1763-23-1

Substance name Perfluorooctanyl sulphonic acid and its salts (PFOS)

Toxicity

PFOS is considered a developmental toxicant by the European Union.¹ In rodent studies, it caused high mortality of offspring, reduced weight gain in surviving pups, and developmental delays.^{2,3} Recent epidemiological investigations into developmental effects associated with background levels of PFOS in pregnant women provide limited support. Apelberg et al. (2007) reported that PFOS in cord blood had a negative association with birth weight and head circumference in babies.⁴ Fei et al. (2007) conducted a similar study but did not observe any association between fetal growth indicators and maternal PFOS levels during pregnancy.⁵ The latter study followed children into early childhood and reported, however, that children whose mothers had the highest PFOS during pregnancy had slight delays in meeting two benchmarks: age at sitting without support and age for certain vocal benchmarks.⁶

In short and long-term tests in adult rats and primates, PFOS results in liver toxicity and mortality.^{2,3}

Exposure

PFOS is listed as a Persistent, Bioaccumulative and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320).³ It was historically used in Scotchgard and other waterproofing materials in children's apparel and furniture.³ According to a 2009 survey, it currently has limited uses in photolithography and as a chemical intermediate in industrial applications. The potassium and ammonium salts of PFOS are used in metal plating and in the manufacture of semiconductors.⁴ PFOS is also a degradation product of many other perfluorinated compounds.⁴ Biomonitoring is still finding widespread detections of PFOS in the serum of the U.S. general population.⁵

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CAS 1806-26-4

Substance name 4-octylphenol

Toxicity

4-octylphenol has been classified as a Category 1 endocrine disruptor by the European Union.¹ Rats exposed to 4-octylphenol during gestation and for three weeks after birth had decreased testicular size and decreased sperm production as adults when compared to unexposed control animals.² Several *in vitro* assays suggest indicate that 4-octylphenol has estrogenic activity.^{3,4}

Exposure

A Dutch study of plastics in children's products found 4-octylphenol in 2 out of 48 polyvinyl chloride plastics.⁵

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CAS 5466-77-3

Substance name 2-ethyl-hexyl-4-methoxycinnamate (also called octinoxate)

Toxicity

2-ethyl-hexyl-4-methoxycinnamate has been classified as a Category 1 endocrine disruptor by the European Union.¹ The compound was found to interfere with the hypothalamic-pituitary-thyroid axis in rats, causing a dose-dependent reduction in thyroid hormones (T3, T4), and thyrotropin (TSH) levels.² 2-ethyl-hexyl-4-methoxycinnamate has demonstrated estrogenic properties in the uterotrophic assay and the MCF-7 breast cancer cell line.³

Exposure

The Danish EPA found 2-ethyl-hexyl-4-methoxycinnamate in 2 out of 5 bed linens⁴ and 2 out of 28 sunscreens marketed for babies.⁴ It is a UV-B filter and is used in many sunscreens, including those marketed for children. It is listed as an ingredient in more than 1700 products including sunscreen, foundation and other facial make-up, lip gloss, and hair products.⁵

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CAS 7439-97-6

Substance name Mercury & mercury compounds

Toxicity

Mercury exists in three forms that have different properties, usage, and toxicity. The three forms are called elemental (or metallic) mercury, inorganic mercury compounds, and organic mercury compounds. Methylmercury and metallic mercury vapor are well known neurotoxicants. Mercury and mercury compounds are listed as developmental hazards by the European Union and the state of California.^{1,2} Animal and human evidence is especially strong for developmental effects of methylmercury and the developing child is considered the most sensitive life stage for exposure.³ Mercury compounds are listed as possible carcinogens by authoritative sources.^{2,4,5}

Exposure

Metallic mercury is used in some thermometers, dental amalgams, fluorescent light bulbs, some electrical switches, mining, and some industrial processes. Inorganic mercury compounds are used in some industrial processes, in the production of other chemicals and in cosmetics in some countries for skin-lightening soap and creams.³ Organic mercury compounds, such as Thimerosal and phenylmercuric acetate, are used as preservatives in pharmaceuticals.³ Metallic mercury has been found in imported jewelry marketed to children in WA State. It is also in button-type batteries used in many children's toys.⁶ The Center for Disease Control and Prevention found widespread detections of both organic and inorganic mercury in biomonitoring the general U.S. population.⁷

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Substance name Molybdenum & molybdenum compounds

Toxicity

Molybdenum is an essential trace nutrient in humans. Molybdenum compounds have caused reproductive and developmental problems in animal studies.¹⁻⁴ Reported effects include male sterility, reduced fetal weight gain, reduced skeletal ossification, and reduced survival of offspring. Evidence from studies in rodents indicates that copper plays a key role in protecting against these effects.⁴ A recent study reported an inverse association between background levels of molybdenum exposure in men and sperm quality and concentration.⁵

Exposure

Molybdenum is a hard metal widely used to add strength and hardness and retard corrosion in metal alloys. It is used in lubricants, in pigments for ceramics and inks and paints.⁷ More recently the semiconductor and battery industry have begun to use molybdenum. Molybdenum was found in a pencil case and school bags in testing of children's school supplies by the Danish EPA.⁶ Biomonitoring in the general U.S. population by the Centers for Disease Control and Prevention (CDC) show that levels in the general population dropped slightly from 1999 to 2004.⁷

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CAS 7440-36-0

Substance name Antimony & Antimony compounds

Toxicity

Antimony trioxide is classified as a carcinogen by authoritative sources.¹⁻⁴ The listings are based on experimental evidence that demonstrates induction of lung tumors in rats following inhalation of antimony trioxide. There are supportive human data which show an excess of mortality from lung cancer among antimony workers, but these data are not considered conclusive.^{2,3,5}

Exposure

Antimony trioxide (ATO) is used as catalyst in the manufacture of polyester fabrics and polyethylene terephthalate (PET) plastics and is used as a synergist to flame retardants in textiles, plastics, paints, adhesives and sealants. Antimony compounds are also used in the manufacture of pigments, paints, glass, pottery, and enamels. Antimony is common at low percentages in metal alloys.⁶

The Danish Environmental Protection Agency (DEPA) detected antimony in their tests of many children's products including perambulator covers, pencil cases, school bags, glitter glue, natural toys, mattress pads and fabric samples such as polyester clothing.⁷ Antimony was found in a DEPA survey of jewelry that included children's jewelry.⁷ Biomonitoring in general U.S. population reported widespread detections in people. Children appear to have higher body burdens than adults.⁸

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CAS 7440-38-2

Substance name Arsenic & Arsenic compounds

Toxicity

Arsenic is classified as a carcinogen by a number of authoritative sources.¹⁻⁴ In humans, arsenic exposure has been linked to lung cancer, bladder cancer, skin cancer, and cancers at several other sites in the body. The state of California has identified it as a reproductive toxicant.⁴

Exposure

Historically inorganic arsenic compounds were used in wood preservatives, other pesticides, medicines, metal alloys, and paint pigments.^{5,6} The Danish EPA found arsenic in children's products including 3 of 4 pencil cases and 5 of 7 school bags.⁷

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Toxicity

Cadmium and cadmium compounds are classified as carcinogens by authoritative sources.¹⁻⁴ Cadmium produces lung and other cancers in laboratory animals by multiple routes of exposures.¹ Studies of people exposed to cadmium have reported excess lung and prostate cancers although co-exposures to other carcinogens often limit the human evidence.¹ It appears that ionic cadmium is genotoxic.¹ Cadmium accumulates in liver and kidney and can cause kidney damage if the levels in the kidney are high enough.^{3,5} Cadmium damages male and female reproductive organs and tissues in rats and mice and is classified as a reproductive hazard by the European Union and the state of California.^{4,7} Young animals exposed to cadmium before birth have shown impaired growth and neurobehavioral effects.^{4,5,7}

Exposure

Cadmium is used primarily in the manufacture of nickel-cadmium batteries. It is also used as pigments for plastics, ceramic, and glass; as a stabilizer for polyvinyl chloride (PVC); and in alloys and coatings on steel and other non-ferrous metals.^{4,5} The Danish EPA detected cadmium in children's school supplies, such as pencil cases and school bags.⁶ A Danish investigation of jewelry from south Asia detected significant amount of cadmium in some "silver" items and demonstrated that cadmium could migrate out of these items in artificial sweat.⁴

References

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CAS 7440-48-4

Substance name Cobalt & Cobalt compounds

Toxicity

Some cobalt compounds are classified as carcinogens by authoritative sources.¹⁻³ Inhalation of cobalt compounds can induce lung and other cancers in rats and mice.^{1,2} Occupational studies are not conclusive but do indicate that cobalt may be an agent of lung cancer in humans.^{1,2,5} Oral exposures to soluble cobalt compounds are associated with testicular atrophy and reduced fertility in male rodents.⁴ There is also a limited literature indicating that cobalt had developmental toxicity in rodents.⁴

Exposure

Cobalt is used in alloys, pigments, and fertilizers; as a drying agent in paints, varnishes and inks; a component in porcelain enamel; and as a catalyst in synthesizing polyester and other materials.⁵ In testing by the Danish EPA, cobalt was found in samples of fabric, in glass and porcelain colors, and at trace levels in school supplies.⁶

References

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http://www.mst.dk/English/Chemicals/Consumer_Products/Surveys-on-chemicals-in-consumer-products.htm.

CAS 25013-16-5

Substance name Butylated hydroxyanisole (BHA)

Toxicity

Butylated hydroxyanisole (BHA) is classified as a carcinogen by authoritative sources.^{1,2,3} Oral exposures induced cancers of the forestomach in rats and mice.^{1,2} BHA is also listed as a Class 1 endocrine disruptor by the European Union.⁴ Their classification is based on evidence of disruption of androgen and thyroid hormonal systems in a number of *in vitro* and *in vivo* tests. In a rat reproduction study, BHA increased relative organ weights of liver, kidney, adrenal gland and thyroid gland; decreased the mating rate; resulted in less males being born; shortened anogenital distances in male offspring; lengthened the time to vaginal patency and preputial separation in female offspring; and had measurable effects on sperm.⁵

Exposure

BHA is used primarily as a antioxidant and preservative in food, food packaging, cosmetics, pharmaceuticals, and in rubber and petroleum products.^{1,2} BHA was reported in many cosmetics in a large survey of use in consumer products.² The highest concentrations were in lipsticks and eye shadows. BHA is listed as an ingredient in baby scalp spray-on sunscreen, diaper rash ointments, and baby oil in an online cosmetics database.⁶ It has also been reported in chewing gum samples.²

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CAS 25154-52-3

Substance name Nonylphenol

Toxicity

Nonylphenol has been classified as a Category 1 endocrine disruptor by the European Union.¹ Uterotrophic assays indicate that nonylphenol has estrogenic activity, and several other lines of evidence suggest that nonylphenol can adversely affect mammalian reproduction.²

Exposure

The Danish EPA found nonylphenol in 1 of 3 pencil erasers³ and 1 of 28 infant sunscreens.⁴ A Dutch study of plastics in children's products found nonylphenol in many samples (mostly polyvinyl chloride).⁵

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CAS 25637-99-4

Substance name Hexabromocyclododecane (HBCD)

Toxicity

Hexabromocyclododecane (HBCD) has been associated with reproductive and developmental effects in laboratory animals. Fertility index was reduced, newborn animal mortality was increased, and the number of primordial follicles in rat ovaries was reduced by exposure to HBCD that was ingested.¹ Oral dosing of rats resulted in changes in thyroid weight, levels of thyroid hormones, and levels of thyroid stimulating hormone.¹ The liver is also a target for HBCD toxicity.¹

Exposure

This substance is listed as a Persistent, Bioaccumulative and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320).² HBCD is a brominated flame retardant that is used for polystyrene and for some fabrics.¹ Its use in child car seats has been reported.¹ HBCD has been found in human breast milk and blood in biomonitoring studies.¹

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CAS 26761-40-0 (also 68515-49-1)

Substance name Diisodecyl Phthalate

Toxicity

Diisodecyl phthalate has been classified as a developmental toxicant by the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction and by the state of California.^{1,2} The National Toxicology Program concluded that there is clear evidence of developmental toxicity.¹ Effects in animals included abnormal development of the fetal skeleton as well as reduced weight gain and survival of the pups.¹

Exposure

The Danish EPA found diisodecyl phthalate in a foam toy.³ Diisodecyl phthalate has also been found in teething rings and other toys.^{4,5}

Monocarboxyisononyl phthalate, a metabolite indicative of diisodecyl phthalate exposure, was found in 89.9 percent of the U.S. population sampled in the NHANES survey.⁶

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CAS 28553-12-0 (also 68515-48-0)

Substance name Diisononyl Phthalate

Toxicity

Diisononyl phthalate has been classified as a developmental toxicant by the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction.¹ The National Toxicology Program concluded that there is some evidence of developmental toxicity in animals including reduced birth weight and abnormal development of the fetal skeleton and kidneys.¹

Exposure

The Danish EPA found diisononyl phthalate in numerous children's products including pacifiers, mittens, soap containers, school supplies, a slimy toy, packaging for cosmetics, 1 of 2 bath toys, and 1 of 2 nursing pillows.² A Dutch study found diisononyl phthalate in polyvinyl chloride in some children's products.³ Monocarboxyisooctyl phthalate, a metabolite indicative of diisononyl phthalate exposure, was found in 95.2 percent of the U.S. population sampled in the NHANES survey.⁴

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